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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,105	03/28/2001	Kalyan Handique	10255-014-999	4325

26171 7590 07/02/2004

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EXAMINER

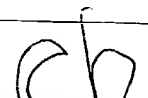
GORDON, BRIAN R

ART UNIT	PAPER NUMBER
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1743

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/819,105	Applicant(s) HANDIQUE ET AL.	
	Examiner Brian R. Gordon	Art Unit 1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 and 14-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 14-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>6-15-04</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Specification

1. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1-9, 13, 21-34, and 38-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Handique et al. US 5,750,015.

Handique et al. discloses an invention that relates to microfabrication and biological reactions in microfabricated devices, and in particular, movement and mixing of biological samples in microdroplets through microchannels. The description of the invention involves I) the design of microscale devices (comprising microdroplet transport channels, reaction chambers, electrophoresis ports, and radiation detectors) using silicon and glass substrates, II) the creation (or definition) of microdroplets having a discrete size, III) movement of discrete microdroplets using a surface-tension-gradient mechanism in which discrete microdroplets are differentially heated and propelled through etched channels, IV) flow control with sealed valves, and V) mixing of biological

samples for reactions. The invention contemplates microscale devices, comprising microdroplet transport channels having hydrophilic and hydrophobic regions, reaction chambers, gas-intake pathways and vents, electrophoresis modules, and detectors, including but not limited to radiation detectors. In some embodiments, the devices further comprise air chambers to internally generate air pressure to split and move microdroplets (i.e. "on-chip" pressure generation).

Electronic components are fabricated on the same substrate material, allowing sensors and controlling circuitry to be incorporated in the same device. The present invention contemplates a method for moving microdroplets, comprising: (a) providing a liquid microdroplet disposed within a microdroplet transport channel etched in silicon, said channel in liquid communication with a reaction region via said transport channel and separated from a microdroplet flow-directing means by a liquid barrier; and (b) conveying said microdroplet in said transport channel to said reaction region via said microdroplet flow-directing means. It is not intended that the present invention be limited by the particular nature of the microdroplet flow-directing means. In one embodiment, it comprises a series of aluminum heating elements arrayed along said transport channel and the microdroplets are conveyed by differential heating of the microdroplet by the heating elements. In one embodiment, said first microdroplet comprises nucleic acid and said second microdroplet comprises a nuclease capable of acting on said nucleic acid. In this embodiment, it is desirable to enhance the mixing within the merged microdroplet. This can be achieved a number of ways. In one embodiment for mixing, after the conveying of step (d), the flow direction is reversed. It is not intended that the

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present invention be limited by the nature or number of reversals. If the flow direction of said merged microdroplet is reversed even a single time, this process increases the mixing of the reactants. The present invention also contemplates a method for restricting fluid flow in a channel, comprising: a) providing: i) a main channel connected to a side channel and disposed within a substrate, ii) meltable material disposed within said side channel and associated with a heating element, and iii) a movement means connected to said side channel such that application of said movement means induces said meltable material to flow from said side channel into said main channel; b) heating said meltable material such that said meltable material at least partially liquifies; and c) applying said movement means such that said liquified meltable material flows from said side channel into said main channel. While the present invention is not limited by the movement means, in one embodiment the movement means is forced air.

Successful mixing can be confirmed by characterization of the product(s) from the reaction. Where product is detected, mixing has been at least partially successful. The invention contemplates, in one embodiment, using electrophoresis to confirm product formation.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 10-12, 14-20, 35-37, and 46-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Handique et al. as applied to claims 1-9, 13, 21-34, and 38-45 above, and further in view of Soane et al. or in the alternative, Southgate.

Handique et al. do not disclose that the device specifically functions in response to sub-sequence and sub pattern controls.

Soane et al. disclose a device for conducting reactions (e.g., sequencing synthesis methods), the different fields connected to the movement area can be applied so as to move specific types of charged molecules into contact with other types of

charged molecules in order to react the molecules and carry out any number of different reaction protocols (processing requests). The electrical connections contacting the movement area are preferably in the form of intelligent integrated circuitry which is interactive with a computer system (host computer) capable of activating the fields in any given manner so as to create precise types of separation of molecules for analysis or combinations of molecules for reaction.

Sophisticated computer programs can be set up in order to provide for synthesis or sequencing protocols of a variety of different types of molecules. For example, different nucleotides can be reacted to form DNA and different amino acids can be reacted to form proteins. These reactions can be carried out at greatly increased speeds as compared with conventional mechanical technologies. In addition to increased speeds, the yield is vastly improved due to the precision with which the reactants can be moved. It is possible to carry out DNA or protein sequencing procedures.

It would have been obvious one of ordinary skill in the art at the time of the invention to program the computer system of Soane et al. to include sub-pattern responses in order expedite the processing of numerous samples with improved precision.

Southgate discloses a microfluidic chemical analysis device that preferably includes a physical enclosure covering its enclosed mechanisms, which comprise the internal chemical, electromechanical, electrical, electronic, and computer assemblies, as well as a power supply. The device preferably includes an operator interface, which

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includes a suitable display of symbol- or language-based information, such as a liquid crystal display, and a keyboard for inputting information, which can be numeric, alphabetical, or alphanumeric. The device also preferably includes a bar-code scanner as well as software for processing such information. Further software that is preferably included with the device include instrument control software dedicated to the bar-code reader as already noted, the sample loader sequencer and sample transfer sequencer, the cassette assay sequencer, the batch transporter loader sequencer, calibration of fluid movement, and regulatory requirements satisfaction control. Software is also preferably included in the device for user help functions, manual sample identification input, and error handler, wherein any perturbations or other perceivable error events are recognized and stored for output with a final result report. Power source used for operating the inventive device is standard line voltage of 100 to 240 Volts, alternating current, at a frequency of 50 Hz to 60 Hz.

It would have been obvious to one of ordinary skill in the art to provide a computer controlled system such as that of Southgate in order to reduce or minimize the possibility of contamination that may arise from the interaction of the technician.

Response to Arguments

Applicant's arguments, see remarks, filed April 26, 2004, with respect to the 102(b) rejections as based upon Southgate, Soane et al., Ramsey, and Parce have been fully considered and are persuasive. The respective 102(b) rejections have been withdrawn.

With respect to the 102(b) rejection as based upon Handique et al., the examiner asserts the reference does disclose the limitation of heating a gas to generate a gas pressure and (b) determining, utilizing at least one internal component, the presence or absence of a micro-droplet at a selected position.

“By heating air trapped inside chambers (180) that are in fluidic communication with the microdroplet transport channel via the gas-intake pathway (150), an increased pressure can be generated.” (column 14, lines 4-9)

“The various components are linked (i.e., in liquid communication) using flow-directing means, including but not limited to, a flow directing means comprising a surface-tension-gradient mechanism in which discrete droplets are differentially heated and propelled through etched channels. Electronic components are fabricated on the same substrate material, allowing sensors and controlling circuitry to be incorporated in the same device. Since all of the components are made using conventional photolithographic techniques, multi-component devices can be readily assembled into complex, integrated systems.” (column 3, last paragraph)

“In another medical diagnostic application, it may be desirable to simply detect the presence or absence of specific allelic variants of pathogens in a clinical sample.” (column 4, lines 24-27)

Conclusion

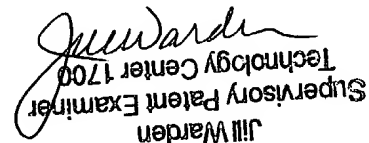
THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian R. Gordon whose telephone number is 571-272-1258. The examiner can normally be reached on M-F, with 2nd and 4th F off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on 571-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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Technology Center 1700

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